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Synthesis of 2-(2-hydroxyaryl)alkenylphosphonium salts from phosphine oxides *via* ring-closing ring-opening approach and their antimicrobial evaluation

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ABSTRACT

A new two-step synthesis of phosphonium salts from phosphine oxides using Grignard reagents is reported. This approach involves a cyclization of *Z*-dialkyl-(diaryl)[2-(5-chloro-2-hydroxyphenyl)-2-phenylvinyl]phosphine oxides under the action of sulfinyl chloride with the formation of 2,2-dialkyl(diaryl)-6-chloro-4-phenyl-2*H*-1,2-benzoxaphosphinin-2-ium chlorides followed by ring opening under the action of organomagnesium compounds. The method was successfully applied to prepare a series of a new phosphonium salts bearing phenolic moiety with a wide range of substituents at phosphorus atom. Synthesized phosphonium salts shows high antibacterial and antifungal *in vitro* activity and low toxicity towards human red blood cell.

1. Introduction

Phosphonium salts are an extensively studied class of organophosphorus compounds. They have found application in asymmetric phase-transfer catalysis,[1–4] as organocatalyst[5] as well as ionic liquids.[6,7] The introduction of phosphonium functionality onto either natural or synthetic frameworks may lead to new pharmaceutically attractive compounds with antitumor[8–12] and antimicrobial activities.[13–15] Recently the structure, synthesis and practical application of polymeric materials containing a quaternary phosphonium moiety as antimicrobial agents have been observed.[16] In addition, some phosphonium salts are able to the reversible inhibition of cholinesterases[16,17] and possess a mitochondrion targeted antioxidant activity.[18–24]

The reactions of P(III) derivatives with alkyl halides or carbonyl compounds in the presence of hydrogen halide are commonly used for the obtaining of the phosphonium salts.[13,14] In such a reactions triphenyl- or tributylphosphines or rarely other trialkyl derivatives are usually applied. A few works on synthesis of phosphonium salts based on the reaction of tertiary phosphines with ortho-quinones[25,26] should also be noted. Recent advances of these synthetic approaches are widely reviewed.[13,14]

Earlier, we have shown by only one example that the reaction of 2-(5-chloro-2-hydroxyphenyl)-2-phenylvinyl diethylphosphine oxide with excess of bromine leads to the cyclic phosphonium salts.[27]

Here, we report a two-step synthesis of the functionally substituted phosphonium salts **9, 10** bearing a hydroxy-group in the position delta to phosphorus from quasiphosphonium salts **2**. This approach has been reported briefly earlier as the conference proceedings without any experimental details.[28]

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